REMARKS

A. The Office Action and Applicant's Amendment and Response

Information Disclosure Statement. The Examiner objected to the information disclosure statement filed June 25, 2002 for failing to comply with 37 C.F.R. 1.98(a) (1 and 2) for the European Search Report references 31 and 32. Applicant has reviewed the references cited in European Search Report references 31 and 32 and notes that all of the references were indeed individually cited and copies of the references were provided in either the Information Disclosure Statement filed June 25, 2002 (foreign patent documents and other document nos. 27-30), or previously in the Information Disclosure Statement filed and July 7, 2000 (other documents nos. 1, 6, 20 and 25), in compliance with 37 C.F.R. 1.98(a) (1 and 2).

Specification. The Amendment at page 12, lines 9-11 is to correct a typographical error by removing "http://" and an unneeded slash from the website address.

The Examiner objected to the abstract for being longer than 150 words. Applicants thank Examiner for bringing this to their attention and have amended the recitation of the abstract to less than 150 words, in compliance with MPEP § 608.01(b).

Claims. For greater clarity, Applicants have amended Claim 1 by deleting "(e)" preceding the "wherein the physiological and/or immunological feature is...."

Additional claim amendments are described in detail hereinbelow.

No new matter is added by any amendment herein.

The Examiner stated that "Claims 1, 2, 5, 8, 11, 12, 16, 22-27 are free of the prior art since the prior art did not teach nor fairly suggest the claimed step of use of antisense to MSX1 and HES1 found in each of the instant method and composition claims." (Office Action, at page 18, Item 11).

No claims were allowed.

The Examiner stated the following reasons for rejection of the claims.

B. Rejection of Claim 5 under 35 U.S.C. § 112, second paragraph

Claim 5 was rejected under 35 U.S.C. § 112, second paragraph, because the claim lacked an antecedent basis for "the neurogenic transcription factor NeuroD1...." Also, Examiner suggested that Claim 5 would be more clearly stated if there was a punctuation mark between the words "glial cell" and "said cell." Applicant has amended Claim 5, at lines 4 and 13, as suggested by the Examiner, to overcome this rejection, which the Examiner is respectfully requested to withdraw.

C. Rejections under 35 U.S.C. § 112, first paragraph

(1) Claims 1, 2, 5, 8, 11, 12, 16 and 22-27 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner based the rejection on the assertion, *inter alia*, that:

> **...The specification as filed does not teach by way of example that any of the obtained cells from the methods disclosed could be considered glial cells. The specification only teaches in Table 1 a defined set of cells having some characteristic of a differentiated neuronal cell, the structure of which is not adequately described therein, and would not appear to have the instantly claimed features of a glial cell. The specification teaches broadly that different characteristics of neuronal cells were evaluated, but does not specify the uniformity of such characteristics amongst or between the cells having different transcription factors and antisense sequences applied, nor how these neuronal cells relate to glial cells. Therefore, it is not clear to one of skill in the art that the cells taught as differentiated neuronal cells have the glial structures now claimed or that a representative number of such glial cells was described by the specification as filed to show that applicant indeed had possession of glial cells at the time the invention was made. The activation of one or several genes in epidermal cells leading to the transcription of one or more neuronal markers or a single physiological response does not indicate that such modified epidermal cells would necessarily have the function of glial cells based on cell acquisition of one or several such morphological features.**

Applicant respectfully disagrees, because this rejection appears to be based on a misunderstanding of the Applicants' claims. Contrary to the Examiner's statement, Applicants' claims are not directed to complete glial cells; rather they involve a

transdifferentiated "cell having *one or more morphological, physiological and/or immunological feature(s) of a glial cell*," as recited in Claims 1, 5 and 11. Furthermore, Applicants' specification describes an actual reduction to practice of the claimed invention.

The analysis of whether the specification complies with the written description requirement calls for the Examiner to compare the scope of the claim with the scope of the description to determine whether the Applicant has demonstrated possession of the claimed invention. MPEP § 2163. Accordingly, consistent with the explicit recitation of Claims 1, 5 and 11 (and implicitly in claims directly or indirectly dependent therefrom), Applicants need only describe transdifferentiated cells having one or more morphological, physiological and/or immunological feature(s) of a glial cell to comply with the written description requirement.

The specification discloses, by way of example, that expression of astroglial marker fibrillary acidic protein (GFAP) or the oligodendroglial maker O4 is a glial-specific feature. (Specification, at page 18, lines 20-22). Furthermore, Claims 1 and 5 recite that the transdifferentiated cells express a marker "selected from the group consisting of GFAP and O4, or a combination of these." The Examiner asserted that "[t]he specification only teaches in Table 1 a defined set of cells having some characteristic of a differentiated neuronal cell...and would not appear to have the instantly claimed features of a glial cell." Contrary to this assertion, Applicants have described an actual reduction to practice, demonstrating that transdifferentiated cells expressing the glial-specific marker protein, GFAP, were actually obtained. As the specification teaches, at page 31, lines 13-16:

> ...staining of treated epidermal cell cultures with antibodies against glial fibrillary acidic protein shows that small percentage (around 5%) of cells also express GFAP. This is an indication that transdifferentiated cells acquire characteristics of astroglial cells, either directly or indirectly.

Thus, the specification does reasonably convey to the skilled artisan that Applicants were in possession of the claimed invention. Possession may be shown where, as here, Applicants have described an actual reduction to practice of an embodiment or a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.

See MPEP § 2163. Applicants claim a transdifferentiated epidermal basal cell having *one or more morphological, physiological and/or immunological feature(s) of a glial cell* and have disclosed that the expression of GFAP and O4 markers as examples of such glial cell features. Applicants have further demonstrated that cells expressing GFAP were actually obtained from practicing the claimed invention. Therefore, Applicants respectfully request the Examiner to withdraw the rejection on this ground.

With respect to Claims 11 and 12 drawn to kits, the Examiner stated that:

> **...The claims drawn to kits containing ingredients for differentiation of epidermal cells to neuronal cells are further not adequately described by the specification as filed because the specification does not teach the structure of glial cells based on the application of the various kit components.**

Claims 11 and 12 are drawn to kits for converting, in vitro, epidermal basal cells into cells *having one or more morphological, physiological and/or immunological feature(s) of a glial cell*. Again, the rejection of the Claims 11 and 12 is premised on the same misunderstanding that the claims are directed to complete glial cells and that the specification does not adequately teach the structure of such glial cells based on application of the various kit components. The specification discloses that the application of the kit components resulted in transdifferentiated epidermal basal cells having one or more morphological, physiological and/or immunological feature(s) of a glial cell, and an actual reduction to practice was demonstrated for transdifferentiated cells expressing GFAP. (Specification, at page 31, lines 13-16). For this reason, and for the reasons stated above, Applicants respectfully request the Examiner to withdraw the rejection on this ground.

The Examiner also stated:

> **The claims read on administration of whole genes or gene fragment from any species of organism, a representative number of species of which is not provided in the specification as filed. It is not clear from the specification as filed what the structures of the fragments are that would function equivalently to the whole growth factor gene.**

While not agreeing with the Examiner, Applicants have deleted the recitation of "[active] fragments" in Claims 1, 2, 5 and 11. Applicants further note that the claims do not

read on a genus of whole genes. The claims recite a Markush group of neurogenic transcription factors consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1.

Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of Claims 1, 2, 5, 8, 11, 12, 16 and 22-27 on this ground.

(2) Claims 1, 2, 5, 8, 11, 12, 16 and 22-27 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to, to make and/or use the invention. The Examiner based this rejection the basis that Applicant had not demonstrated possession of glial cells in the specification. Applicants respond to this rejection as provided above. In addition, the Examiner stated that

> **As argued previously and above, the types of cells taught in the instant specification are defined as neuronal cells based on a few criteria as morphological extensions, however, such criteria do not enable one of skill in the art to make and use glial cells. Absent more specific guidance in the art for which genes must be expressed in epidermal basal cells, under what cell culture conditions, with an expectation of certain concrete indicates of glial cell pathology, one of skill in the art would necessary practice an undue amount of experimentation to make and use the breadth [sic] of claimed transdifferentiated glial cells and methods of making said cell.**

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation. MPEP 2164.01. In Example VI of the specification, for example, Applicants disclosed working examples of various combinations of the claimed neurogenic bHLH and/or Zn-finger transcription factors and MSX1 and/or HES1 to transdifferentiate epidermal basal cells.

In Example VI, the specification described the results of experiments that positively showed expression of GFAP in the transdifferentiated epidermal basal cells for a number of exemplary transfections using combinations of neurogenic genes and antisense oligonucleotides, in accordance with the claimed inventions. These resulted in around 5% of cells expressing GFAP, a known physiological and/or immunological feature of a glial cell

(Specification, e.g., at page 18, lines 18-22; at page 19, lines 5-7; and at page 31, lines 13-16). The teachings in the specification and the disclosure of working examples provide an enabling disclosure of a transdifferentiated epidermal basal cell having *one or more morphological, physiological and/or immunological feature(s) of a glial cell.*

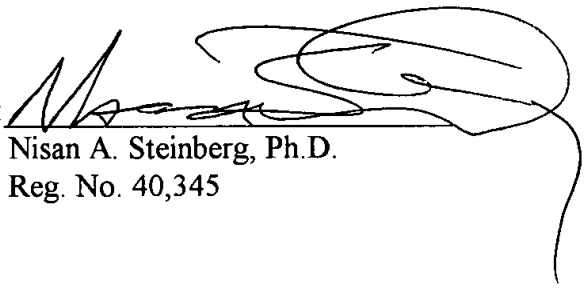
Applicants respectfully submit that an enabling disclosure for the full scope of the claims is provided. Enablement is satisfied where, as here, there is no reason to doubt that the working examples bear a reasonable correlation to the entire scope of the claim. See MPEP § 2164.01(b). Applicant is not required to prove enablement for other members of a claimed genus where there are no adequate reasons advanced by the Examiner to establish that a person skilled in the art could not use the genus, as a whole, without undue experimentation. See MPEP § 2164.02.

Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of Claims 1, 2, 5, 8, 11, 12, 16 and 22-27 on this ground.

CONCLUSION

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. Early notice to that effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,

By: 
Nisan A. Steinberg, Ph.D.
Reg. No. 40,345

SIDLEY AUSTIN BROWN & WOOD LLP
555 West Fifth Street, Suite 4000
Los Angeles, California 90013
Ofc: 213/ 896-6665
Fax: 213/ 896-6600